## REMARKS

Claims 1, 3, 9-13, 15, 17-21, 23, 25-26, 29-31, 33, and 35-39 are pending in the application.

### *Acknowledgment of the Examiner's Withdrawal of Certain Rejection*

Applicants gratefully acknowledge the Examiner's withdrawal of the previous rejection of claims 1, 3-5, 9-13, 15, 17-21, 23, 25-27, 29-31, 33, and 35-39 under 35 U.S.C. § 112, first paragraph as not being enabled.

### *Rejection of Claims 1, 3, 9-13, 15, 17-21, 23, 25-26, 29-31, 33, and 35-39 Under 35 U.S.C. § 103*

The Examiner has maintained the rejection of claims 1, 3, 9-13, 15, 17-21, 23, 25-26, 29-31, 33, and 35-39 as being unpatentable over Kerwin *et al.* (U.S. Patent 5,929,031) in view of Hagiwara *et al.* (U.S. Patent No. 6,165,467), Packer *et al.* (*Methods Enzymol*, 186: 41-42 (1990)) and Akers (*J. Par. Sci. Tech.* 36:222-228 (1982)). The Examiner relies on Kerwin *et al.* for teaching that one or more chelators can be used in a formulation. The Examiner relies on Hagiwara *et al.* for teaching that human monoclonal antibodies have an undesirable property that they easily aggregate and precipitate in a solution state. The Examiner relies on Packer *et al.* for teaching that DEF suppresses iron-dependent generation of OH from $H_2O_2$. The Examiner relies on Akers for teaching that the use of a combination of antioxidants in the same formulation produces a synergistic effect. The Examiner asserts that it would have been obvious to one of skill in the art that "the use of DTPA and DEF would stabilize a composition comprising a human monoclonal antibody" in view of the cited references. Additionally, the Examiner asserts that "since the concentration range of a chelating agent taught by Kerwin et al. is 0-200 μM, which overlaps with the concentration ranges of DTPA and DEF recited in claims 1 and 27, a prima facie case of obviousness exists."

Applicants respectfully traverse this rejection for at least the following reasons, as well as those previously made of record. Specifically, with respect to the Examiner's assertion that the concentration range taught by the primary reference, Kerwin *et al.* (*i.e.*, 0-200 μM = 0-0.2mM), overlaps with the claimed concentration ranges of DTPA and DEF, Applicants respectfully note that Kerwin *et al.* is completely silent with respect to the use of DEF, let alone at a particular concentration range or in combination with DTPA. Thus, the teachings of Kerwin *et al.* can not

be applied to the claimed concentration range of 0.02 mM to 0.5 mM for DEF. Indeed, how could Kerwin *et al.* render obvious the use of chelator which is not taught, at a particular concentration range, which is also not taught? Moreover, the only reference cited by the Examiner which does teach DEF (i.*e.*, Packer *et al.*) provides no guidance with respect to an appropriate concentration of DEF to include in a composition.

Accordingly, since none of the cited references, either alone or in combination, teach or suggest the presently claimed compositions (*i.e.*, a composition comprising an antibody (or fragment thereof) formulated with DTPA and DEF), let alone the particularly claimed concentration ranges of DTPA and DEF, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness. As such, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

***Rejection of Claims 1, 3, 9-10, 12-13, 15, 17-21, 23, 25-26, 29-31, 33 and 35-39 Under 35 U.S.C. § 103***

The Examiner has maintained the rejection of claims 1, 3, 9-10, 12-13, 15, 17-21, 23, 25-26, 29-31, 33 and 35-39 as being unpatentable over Foster *et al.* (U.S. Patent 5,217,954) in view of Hagiwara *et al.* (U.S. Patent No. 6,165,467), Packer *et al.* (*Methods Enzymol*, 186: 41-42 (1990)) and Akers (*J. Par. Sci. Tech.* 36:222-228 (1982)). The Examiner relies on Foster *et al.* for teaching the use of a pharmaceutical formulation comprising a protein, bFGF, a stabilizing chelator, such as DTPA or EGTA to protect bFGF from oxidation. The Examiner further relies on Foster *et al.* for teaching an agent for tonicity, a preservative or other auxillaries, such as mannitol, glycerol, sodium chloride or Tris. The Examiner relies on Hagiwara *et al.*, Packer *et al.* and Akers for the reasons discussed above. The Examiner concludes that it would have been obvious to one of skill in the art that "the use of DTPA and DEF would stabilize a composition comprising a human monoclonal antibody" in view of the cited references. Additionally, the Examiner asserts that "since the concentration range of a chelating agent taught by Foster et al. is equivalent to about 0.025 mM to 50 mM for DTPA and 0.018 to 36 mM for DEF, which overlaps with the concentration ranges of DTPA and DEF recited in claims 1 and 27, a prima facie case of obviousness exists."

Applicants respectfully traverse this rejection for at least the following reasons, as well as those previously made of record. Specifically, with respect to the Examiner's assertion that the concentration range taught by the primary reference, Foster *et al.* overlaps with the claimed

concentration ranges of DTPA and DEF, Applicants respectfully note that Foster *et al.* do not teach or suggest the use of DEF, let alone at a particular concentration range or in combination with DTPA. In fact, DEF is not even mentioned in Foster *et al.* Moreover, the only reference cited by the Examiner which does teach DEF (i.*e.*, Packer *et al.*) provides no guidance with respect to an appropriate concentration of DEF to include in a composition. Accordingly, based on the teachings of Foster *et al.*, it certainly would not have been obvious to have combined DTPA with DEF, let alone at the specific concentration ranges claimed by Applicants, which also are not taught or suggested by the prior art.

Accordingly, since none of the cited references, either alone or in combination, teach or suggest the presently claimed compositions (*i.e.*, a composition comprising an antibody (or fragment thereof) formulated with DTPA and DEF), let alone the particularly claimed concentration ranges of DTPA and DEF, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness. As such, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

## CONCLUSION

In view of the foregoing, entry of the amendments and remarks herein, reconsideration and withdrawal of all rejections, and allowance of the instant application with all pending claims are respectfully solicited. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

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Respectfully submitted,

By _____

Jill Gorny Sloper
Registration No.: 60,760
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant